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Abstract

Recently there has been a lot of interest in the medical and lay press concerning exposure to mercury and its potential toxic effects. Mercury is a naturally occurring metallic element, which can be found as Hg or inorganic and organic salts. In this article we will review the risks of exposure and toxicity of each of the forms of mercury, including some of the current guidance concerning the risks of mercury toxicity from eating fish, dental amalgam and vaccinations containing mercury (thiomersal) preservatives.

Keywords

mercury, current, answering, controversies, about

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Mercury – answering some of the current controversies about it

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ABSTRACT Recently there has been a lot of interest in the medical and lay press concerning exposure to mercury and its potential toxic effects. Mercury is a naturally occurring metallic element, which can be found as Hg or inorganic and organic salts. In this article we will review the risks of exposure and toxicity of each of the forms of mercury, including some of the current guidance concerning the risks of mercury toxicity from eating fish, dental amalgam and vaccinations containing mercury (thiomersal) preservatives.

KEYWORDS Dental amalgam, ethylmercury, methylmercury, mercury, thiomersal

LIST OF ABBREVIATIONS central nervous system (CNS), elemental mercury (Hg), European Medicines Evaluation Agency (EMA), Food and Drug Administration (FDA), Health Protection Agency (HPA), World Health Organisation (WHO)

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ELEMENTAL MERCURY

Elemental mercury (Hg) is a metallic liquid under normal conditions, and has been used in thermometers and sphygmomanometers. Ingestion of liquid elemental mercury is of low toxicity, since it is very poorly absorbed from the gastrointestinal tract. Therefore broken oral or rectal thermometers are usually of little toxicological significance, unless the patient has significantly reduced gastrointestinal transit time, or has ingested very large amounts of elemental mercury. However, if the contents are spilled onto a surface such as a carpet and the vapour is then inhaled over a period of time, systemic absorption and toxicity can occur. It is important that a vacuum cleaner is not used to clean up spilt elemental mercury, due to volatilisation of the mercury and inhalation of the vapour. Spilt elemental mercury can be cleaned up using specialised kits available from most chemists and these include instructions on its safe disposal. It is poorly absorbed following dermal contact.

Toxicity from elemental mercury occurs from volatilisation of significant quantities since it is freely absorbed through the respiratory tract epithelium. Initial symptoms include nausea, vomiting, acute breathlessness, pyrexia, headache and visual disturbances. Patients may also complain of a metallic taste and associated hypersalivation. Respiratory symptoms can progress to pulmonary oedema and respiratory failure. Patients will require good supportive care, with ventilatory support if significant respiratory symptoms occur. Blood and

urinary mercury concentrations should be obtained and chelation therapy may be required, following discussion with a clinical toxicologist. Patients who develop severe respiratory symptoms and survive, may develop late sequelae, including interstitial fibrosis and residual restrictive pulmonary disease

Chronic exposure to elemental mercury can lead to non-specific symptoms, which include gastrointestinal disturbances, headache and neurological features including depression, irritability, insomnia, confusion, forgetfulness and intellectual deterioration. Chronic exposure can occur following repeated oral ingestion of low concentrations of mercury or by wrongly using a vacuum cleaner to clean up elemental mercury spillages, where the mercury continues to be vaporised each time it is used. Blood and urine mercury concentrations should be measured following discussion with a clinical toxicologist; chelation therapy may be required.

ORGANIC MERCURY SALTS

Organic mercury salts have previously been used as fungicides, but significant exposure to organic mercury salts in humans usually occurs due to ingestion of methylmercury in fish and ethylmercury when thiomersal is used as a preservative in vaccinations. Organic mercury salts are readily absorbed from the gastrointestinal tract, with up to 90% absorption. Since the risk of exposure and therefore toxicity differs between the two organic mercury salts, each will be discussed separately.

Methylmercury

Bacteria metabolising inorganic mercury salts produce methylmercury. Accumulation can occur in fish and shellfish, with higher concentrations in fish higher in the food chain, where there is contamination of water with industrial effluent containing inorganic mercury salts. Methylmercury, when ingested in contaminated fish, has a longer half-life of approximately 50 days, so that accumulation can occur in people who ingest large amounts of fish. Specific amino acid transporters can transport methylmercury across the blood-brain barrier, leading to CNS accumulation. Focal neurological toxicity can occur, and the visual cortex and cerebellum are particularly at risk. The evidence for neurological toxicity in adults from fish is inconclusive. In a Faeroese population, who ingest large amounts of whale meat, exposure to higher concentrations of methylmercury was reported to be associated with deficits in attention, language and memory. However, in this study, ingestion of higher concentrations of polychlorinated biphenyls in whale meat was a confounding factor. Recent cardiological studies have shown that fish containing high quantities of omega-3 fish oils, is associated with a reduction in cardiovascular risk and patients are recommended to eat up to four portions of oily fish per week. This will increase the risk of methylmercury exposure, and this cardiovascular benefit of omega-3 fish oils outweighs the risk of methylmercury toxicity. Some fish, such as salmon, have been shown to have lower concentrations of methylmercury than tuna or swordfish and over the counter preparations containing fish oils have been shown not to contain significant concentrations of methylmercury.

The amino acid transporters are also present in the placenta, and thus maternal-foetal transfer of methylmercury can occur, leading to foetal accumulation. Previous studies have shown that foetal brain accumulation is more diffuse and may lead to subsequent cerebral palsy, deafness, blindness and neurological developmental delay. Due to this risk of foetal neurological toxicity of methylmercury, the WHO in 2003 issued advice that the recommended weekly intake of methylmercury in pregnant women should be reduced from 3.3 to 1.6 µg/kg body weight. Further guidance from the US FDA has recommended that pregnant women limit their intake to one portion of fish per week. However given the long half-life of methylmercury, this advice will mean that women who have eaten large amounts of fish prior to pregnancy will still be placing the foetus at risk of methylmercury toxicity. There is currently no guidance on the amount of fish or methylmercury ingestion that women should follow before becoming pregnant, although it is logical that the advice for pregnant women should be followed with a six month lower fish consumption period.

Ethylmercury

Thiomersal has previously been used as a preservative in vaccinations, and is metabolised to form ethylmercury. The amount of thiomersal previously used in vaccines was 12.5 to 25 µg per 0.5 ml vaccine, and studies have shown an increase in ethylmercury concentrations of up to 50-fold, with the risk increasing with multiple vaccinations. The risks associated with elevated ethylmercury concentrations following vaccinations remains controversial. Ethylmercury has less neurotoxicity than methylmercury, since there is no specific uptake mechanism across the blood-brain barrier, and it has a shorter half-life. Previous studies have suggested a risk of neuro-developmental delays following vaccination with vaccines containing thiomersal, although the data is not robust and is inconclusive. Additionally, following the removal of thiomersal from vaccines, there have been population studies to support a causative role of ethylmercury in developmental delay. Despite the lack of evidence for a direct causative neurological toxic effect of thiomersal, and therefore ethylmercury, the EMEA and HPA have issued guidance in 2004, which acknowledges the lack of evidence of a neurological toxicity from thiomersal but recommends that alternative preservatives are used in future vaccine production.

INORGANIC MERCURY SALTS

Inorganic mercury salts, such as mercuric chloride (HgCl_2) and mercuric sulphate (HgSO_4) have been used in topical medical preparations as anti-microbial agents and for skin whitening. Topical application of inorganic mercuric salts can lead to skin irritation, vesication and corrosive burns. The risk of localised toxicity is dependent on the solubility of the mercury salt, and is greater for mercuric chloride. Following dermal exposure to inorganic mercury salts, the area should be thoroughly irrigated with water and any resultant corrosive burns should be treated conventionally.

Oral ingestion of inorganic mercury salts causes direct corrosive effects on gastrointestinal tract, leading to haemorrhage, massive fluid loss and shock. Approximately 10% of inorganic mercury is absorbed from the gastrointestinal tract following oral ingestion, and the kidney is particularly at risk of toxicity, and acute renal failure can result. This is due in part to hypovolaemia secondary to the gastrointestinal effects and also a direct toxic effect of mercury on the renal tubules. In patients who present early following ingestion, where there are gastrointestinal corrosive features, gut decontamination with gastric lavage and/or whole bowel irrigation should be considered. Meticulous supportive care is required with adequate fluid resuscitation, upper gastrointestinal endoscopy and renal replacement if appropriate. Blood and urine mercury concentrations should be measured, and the need for chelation discussed with a clinical toxicologist.

DENTAL AMALGAM

The majority of dental fillings undertaken in the United Kingdom still use amalgam for the filling. The mercury contained in the dental amalgam is a mixture of elemental mercury (60–70%) and inorganic mercuric salts. Concerns have been raised as to whether patients with numerous fillings should have them removed, and replaced with non-amalgam fillings. The main risk with dental amalgam is to dental practitioners and their staff, since the mercury has to be heated to liquidise it prior to the procedure. Therefore dental practitioners are at risk of inhaling significant quantities of elemental mercury vapour if safe working practices are not in place. From a patient's perspective, there have been previous studies that have concluded that there is no correlation between the number of dental fillings and blood and urinary mercury concentrations. Additionally there is no risk during the insertion of dental fillings. However, removal of dental amalgam could potentially put patients at risk of mercury toxicity. During the removal, the fillings are drilled out which creates fine particulate matter, containing both elemental mercury and inorganic mercury salts. Depending on the size of the particulate matter, this can be inhaled, oxidised and lead to mercury toxicity. Therefore the advice is that the insertion of amalgam in dental fillings does not pose a risk to patients and that the removal of dental amalgam may pose a greater risk than leaving the dental amalgam *in situ*.*

Poisoning with mercury and its salts can produce both serious acute and potentially fatal toxicity and significant

long-term neurological sequelae. Prevention of mercury toxicity is better, more rational and easier than its treatment. Removal of thiomersal in vaccinations, replacement of mercury containing thermometers and sphygmomanometers, and advice concerning ingestion of fish, are reducing the risk of exposure to significant amounts of mercury. There is no evidence for toxicity from dental amalgam fillings and that the removal of dental amalgam could potentially pose a greater risk to patients than leaving the fillings *in situ*.

KEYPOINTS

- Elemental mercury is non-toxic when ingested, but inhalation of elemental mercury vapour can be associated with toxicity.
- There is no conclusive evidence in adults of neurotoxicity with repeated ingestion of methylmercury, which is produced by bacterial metabolism of organic mercury salts and accumulated in fish.
- Thiomersal has been removed as a vaccine preservative since it is metabolised to ethylmercury, but there is no conclusive evidence of associated neurotoxicity.
- Inorganic mercury salts can cause severe toxicity and death when ingested.
- Mercury containing dental amalgam does not give rise to mercury poisoning in patients, but may be an environmental hazard for dental staff.

FURTHER READING

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*Editor's Note

Amalgam fillings containing mercury are so common that cremation gives rise to mercury emissions estimated to account for 16% of current UK emissions. Mercury emissions in the UK have fallen from 31.6 tonnes in 1990 to 8 tonnes in 2002, but to ensure further reductions, the UK government issued statutory guidelines in January

2006 that new crematoria must be fitted with mercury control equipment and established crematoria must reduce mercury emissions by 50% by 2012. Other European countries and the USA are taking similar precautions.

(See <http://www.defra.gov.uk/news/2005/050110a.htm>)